What is claimed is:

1. A method for treating axonal degeneration of the peripheral nervous system comprising:

administering to a patient a compound of the formula:

M^1-AA^2-AA^1-CO-NR_3R_4

a pharmaceutically acceptable salt or prodrug thereof, wherein

M^1 is selected from the group consisting of H, NH_2-CO-, NH_2-CS-, NH_2-SO_2-, X-NH-CO-, X_2N-CO-, X-NH-CS-, X_2N-CS-, X-NH-SO_2-, X_2N-SO_2-, X-CO-, X-CS-, X-, Y-SO_2-, Y-O-CO-, Y-O-CS-, morpholine-CO-, and biotinyl;

X is selected from the group consisting of H, C_{1-10} alkyl, C_{3-15} cyclized alkyl, C_{1-10} fluoroalkyl, C_{1-10} alkyl substituted with J, C_{1-10} fluoroalkyl substituted with J, 1-admantyl, 9-fluorenyl, phenyl, phenyl monosubstituted with K, phenyl disubstituted with K, phenyl trisubstituted with K, naphthyl, naphthyl monosubstituted with K, naphthyl disubstituted with K, naphthyl trisubstituted with K, C_{1-10} fluoroalkyl with an attached phenyl group, C_{1-10} alkyl with an attached phenyl group, C_{1-10} alkyl with two attached phenyl groups, C_{1-10} alkyl with an attached phenyl group substituted with K, C_{1-10} alkyl with two attached phenyl groups substituted with K, C_{1-10} alkyl with an attached naphthyl group, C_{1-10} alkyl with an attached naphthyl group substituted with K, C_{1-10} alkyl with an attached phenoxy group, and C_{1-10} alkyl with an attached phenoxy group substituted with K on the phenoxy group, and C_{1-10} alkyl monosubstituted with M^2;

Y is selected from the group consisting of C_{1-10} alkyl, C_{3-15} cyclized alkyl, C_{1-10} fluoroalkyl, C_{1-10} alkyl substituted with J, C_{1-10} fluoroalkyl substituted with J, 1-admantyl, 9-fluorenyl, phenyl, phenyl monosubstituted with K, phenyl disubstituted with K, phenyl trisubstituted with K, naphthyl, naphthyl monosubstituted with K, naphthyl disubstituted with K, naphthyl trisubstituted with K, C_{1-10} fluoroalkyl with an attached phenyl group, C_{1-10} alkyl with an attached phenyl group, C_{1-10} alkyl with two attached phenyl groups, C_{1-10} alkyl with an attached phenyl group substituted with K, C_{1-10} alkyl with two attached phenyl groups substituted with K, C_{1-10} alkyl with an attached naphthyl group, C_{1-10} alkyl

with an attached naphthyl group substituted with K, C_{1-10} alkyl with an attached phenoxy group, and C_{1-10} alkyl with an attached phenoxy group substituted with K on the phenoxy group, M^2, and C_{1-10} alkyl monosubstituted with M^2;

M^2 is selected from the group consisting of 2-furyl, 2-tetrahydrofuryl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 2-quinolinyl, 1-tetrahydroquinolinyl, 1-isoquinolinyl, 2-tetrahydroisoquinolinyl, and $-N(CH_2CH_2)_2O$;

J is selected from the group consisting of halogen, CO_2H, OH, CN, NO_2, NH_2, C_{1-10} alkoxy, C_{1-10} alkylamino, C_{2-12} dialkylamino, C_{1-10} alkyl-O-CO-, C_{1-10} alkyl-O-CO-NH-, C_{1-10} alkyl-S-, and $-N(CH_2CH_2)_2O$;

K is selected from the group consisting of halogen, C_{1-10} alkyl, C_{1-10} perfluoroalkyl, C_{1-10} alkoxy, phenoxy, NO_2, CN, OH, CO_2H, amino, C_{1-10} alkylamino, C_{2-12} dialkylamino, C_{1-10} acyl, and C_{1-10} alkoxy-CO-, and C_{1-10} alkyl-S-, and $-N(CH_2CH_2)_2O$;

AA^1 and AA^2 side chain blocked or unblocked amino acids with the L configuration, D configuration, or no chirality at the α-carbon selected from the group consisting of alanine, valine, leucine, isoleucine, proline, methionine, methionine sulfoxide, phenylalanine, tryptophan, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, phenylglycine, beta-alanine, norleucine, norvaline, alpha-aminobutanoic acid, epsilon-aminocaproic acid, citrulline, hydroxyproline, ornithine, homoarginine, sarcosine, indoline 2-carboxylic acid, 2-azetidinecarboxylic acid, pipecolinic acid (2-piperidine carboxylic acid), O-methylserine, O-ethylserine, S-methylcysteine, S-ethylcysteine, S-benzylcysteine, NH_2-$CH(CH_2CHEt_2)$-CO_2H, alpha-aminoheptanoic acid, NH_2-$CH(CH_2$-1-naphthyl)-CO_2H, NH_2-$CH(CH_2$-2-naphthyl)-CO_2H, NH_2-$CH(CH_2$-cyclohexyl)-CO_2H, NH_2-$CH(CH_2$-cyclopentyl)-CO_2H, NH_2-$CH(CH_2$-cyclobutyl)-CO_2H, NH_2-$CH(CH_2$-cyclopropyl)-CO_2H, trifluoroleucine, 4-fluorophenylalanine, lysine substituted on the epsilon nitrogen with a biotinyl group, hexafluoroleucine, and NH_2-CHR^2-CO_2H;

R^2 is selected from the group consisting of C_{1-10} branched and unbranched alkyl, C_{1-10} branched and unbranched cyclized alkyl, and C_{1-10} branched and unbranched fluoroalkyl;

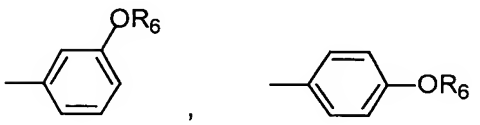
R^3 and R^4 are selected independently from the group consisting of

a) H, C_{1-20} alkyl, C_{1-20} cyclized alkyl, C_{1-20} alkyl with a phenyl group attached to the C_{1-20} alkyl, C_{1-20} cyclized alkyl with an attached phenyl group, C_{1-20} alkyl with an attached phenyl group monosubstituted with K, C_{1-20} alkyl with an attached phenyl group disubstituted with K, C_{1-20} alkyl with an attached phenyl group trisubstituted with K, C_{1-20} cyclized alkyl with an attached phenyl group monosubstituted with K, C_{1-10} alkyl with a morpholine [-N(CH_2CH_2)O] ring attached through nitrogen to the alkyl, C_{1-10} alkyl with a piperidine ring attached through nitrogen to the alkyl, C_{1-10} alkyl with a pyrrolidine ring attached through nitrogen to the alkyl, C_{1-20} alkyl with an OH group attached to the alkyl, -$CH_2CH_2OCH_2CH_2OH$, C_{1-10} with an attached 4-pyridyl group, C_{1-10} with an attached 3-pyridyl group, C_{1-10} with an attached 2-pyridyl group, C_{1-10} with an attached cyclohexyl group, -NH-CH_2CH_2-(4-hydroxyphenyl), -NH-CH_2CH_2-(3-indolyl);

b) -$CH_2CH(OH)$-R^5, and

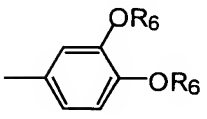
c) -$(CH_2)_n$-R^7;

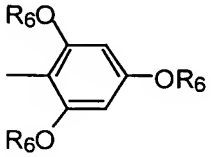
R^5 is selected from the group consisting of phenyl, phenyl monosubstituted with J, phenyl disubstituted with J, phenyl trisubstituted with J, pentafluorophenyl,



,

,



,


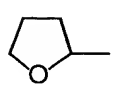
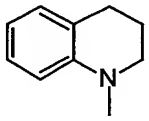
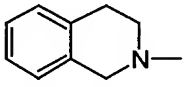
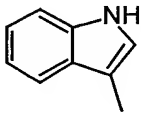
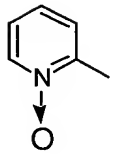
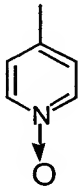
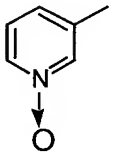
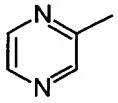
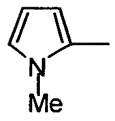
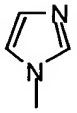
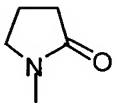
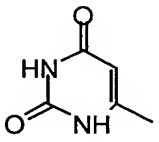
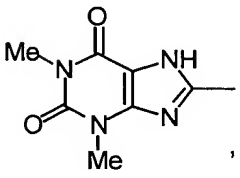
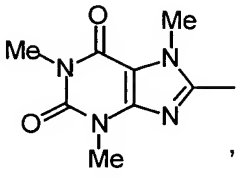
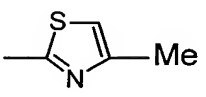
,

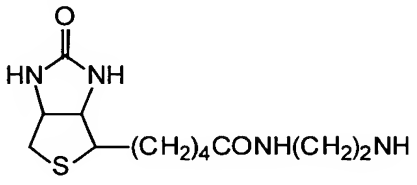
1-naphthyl, 1-naphthyl monosubstituted with J, 1-naphthyl disubstituted with J, 2-naphthyl, 2-naphthyl monosubstituted with J, 2-naphthyl disubstituted with J, 2-pyridyl, 2-quinolinyl, and 1-isoquinolinyl;

R^6 is selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkyl substituted with phenyl, phenyl, and phenyl substituted with J;

n = 1-6;

R^7 is selected from the group consisting of 2-furyl, 2-furyl monosubstituted with J, 2-pyridyl, 2-pyridyl monosubstituted with J, 3-pyridyl, 3-pyridyl monosubstituted with J, 4-pyridyl, 4-pyridyl monosubstituted with J, 2-quinolinyl, 2-quinolinyl monosubstituted with J, 1-isoquinolinyl, 1-isoquinolinyl monosubstituted with J,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

and 

in an amount sufficient to inhibit axonal degeneration.

2. The method of claim 1, wherein the axonal degeneration of the peripheral nervous system is related to idiopathic peripheral neuropathies, peripheral neuropathies due to genetic mutations, peripheral neuropathies associated with uremia, rheumatologic diseases, liver diseases, infections, axonal degeneration secondary to primary demyelinating disorders, inflammatory demyelinating neuropathies, multiple sclerosis, and chronic spinal cord degenerations.

3. A method of claim 1, wherein:

M^1 is selected from the group consisting of X-NH-CO- and Y-O-CO-;

AA^2 is selected from the group from the group consisting of leucine, valine, isoleucine, alanine, and alpha-aminobutanoic acid;

AA^2 is selected from the group from the group consisting of leucine, valine, isoleucine, alanine, alpha-aminobutanoic acid, norvaline, and phenylalanine;

X is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkyl with an attached phenyl group, C_{1-10} alkyl with an attached phenyl group substituted with K, C_{1-10} alkyl with an attached naphthyl group, C_{1-10} alkyl with an attached naphthyl group substituted with K, C_{1-10} alkyl with an attached phenoxy group, and C_{1-10} alkyl with an attached phenoxy group substituted with K on the phenoxy group;

Y is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkyl with an attached phenyl group, C_{1-10} alkyl with an attached phenyl group substituted with K, C_{1-10} alkyl with an attached naphthyl group, C_{1-10} alkyl with an attached naphthyl group substituted with K, C_{1-10} alkyl with an attached phenoxy group, and C_{1-10} alkyl with an attached phenoxy group substituted with K on the phenoxy group.

4. The method of claim 1, wherein the compound is selected from the group consisting of:

Z-Leu-Nva-CH_2-2-pyridyl,

Z-Leu-Abu-$CH_2CH(OH)C_6F_5$,

Z-Leu-Phe-$(CH_2)_2Ph$,

Z-Leu-Abu-$CH_2CH(OH)C_6H_4$-3-$OC_6H_4(3\text{-}CF_3)$,

Z-Leu-Abu-$CH_2CH(OH)C_6H_4(4\text{-}OCH_2Ph)$,

Z-Leu-Abu-$CH_2CH(OH)C_6H_4$(4-OPh),

Z-Leu-Phe-CH_2-2-quinolinyl,

Z-Leu-Abu-$(CH_2)_2C_6H_4$(3-OCH3),

Z-Leu-Abu-$(CH_2)_2C_6H_4$(4-OCH3),

Z-Leu-Abu-$CH_2CH(OH)$-1-$C_{10}H_7$,

Z-Leu-Phe-$(CH_2)_3$-4-morpholinyl,

Z-Leu-Abu-$(CH_2)_2C_6H_4$(2-OCH_3),

Z-Leu-Abu-CH_2-2-quinolinyl,

Z-Leu-Abu-$(CH_2)_3$-4-morpholinyl (AK295),

Z-Leu-Abu-$(CH_2)_2$-2-(N-methylpyrrole),

Z-Leu-Phe-$CH_2CH(OH)C_6H_4$-3-OC_6H_4(3-CF_3),

Z-Leu-Abu-$(CH_2)_2C_6H_5$,

Z-Leu-Phe-Et,

Z-Leu-Abu-$CH_2CH(OC_2H_5)_2$,

Z-Leu-Phe-$CH_2CH(OH)C_6H_4$(4-OPh),

Z-Leu-Phe-$CH_2CH(OH)C_6H_4$(4-OCH_2Ph),

Z-Leu-Abu-$CH_2C_6H_5$,

Z-Leu-Phe-$(CH_2)_2$NH-biotinyl,

Z-Leu-Phe-$(CH_2)_3$-2-tetrahydroisoquinolinyl,

Z-Leu-Abu-$CH_2CH(OH)C_6H_3$(3,4-$(OCH_2Ph)_2$),

Z-Leu-Abu-$CH_2CH(OH)C_6H_4$(4-OCH_3),

Z-Leu-Nva-$(CH_2)_3$-4-morpholinyl,

Z-Leu-Abu-CH_2-1-isoquinolinyl,

Z-Leu-Abu-Et,

Z-Leu-Abu-$CH_2CH(OH)C_6H_4$-3-OC_6H_3(3,4-Cl_2),

Z-Leu-Abu-Me,

Z-Leu-Abu-$(CH_2)_3$-1-imidazolyl,

Z-Leu-Abu-$(CH_2)_2$-3-indolyl,

Z-Leu-Abu-$(CH_2)_3$-2-tetrahydroisoquinolinyl,

Z-Leu-Abu-CH_2-2-tetrahydrofuryl,

Z-Leu-Abu-$CH_2CH(OH)C_6H_4(4\text{-}N(CH_3)_2)$,

Z-Leu-Phe-*n*-Pr,

Z-Leu-Abu-$CH_2CH(OH)\text{-}2\text{-}C_{10}H_7$,

Z-Leu-Phe-Me,

Z-Leu-Abu-$CH_2CH(OH)C_6H_4(3\text{-}CF_3)$,

Z-Leu-Abu-$(CH_2)_3$-1-tetrahydroquinolinyl,

Z-Leu-Abu-$(CH_2)_2C_6H_4(4\text{-}OH)$,

Z-Leu-Abu-$CH_2CH(OH)C_6H_2(3,4,5\text{-}(OCH_3)_3)$,

Z-Leu-Phe-$(CH_2)_3$-1-tetrahydroquinolinyl,

Z-Leu-Abu-$(CH_2)_2$-2-pyridyl,

Z-Leu-Abu-$CH_2\text{-}C_6H_7(1,3,3\text{-}(CH_3)_3\text{-}5\text{-}OH)$,

Z-Leu-Phe-$CH_2CH(OH)C_6H_4(3\text{-}CF3)$,

Z-Leu-Phe-$CH_2CH(OH)C_6H_3(3,4\text{-}(OCH_2Ph)_2)$,

Z-Leu-Abu-$(CH_2)_5OH$,

Z-Leu-Abu-$CH_2CH(OCH_3)_2$,

Z-Leu-Phe-$CH_2CH(OH)C_6H_4\text{-}3\text{-}OC_6H_3(3,4\text{-}Cl_2)$,

Z-Leu-Phe-$CH_2CH(OH)C_6H_4(3\text{-}OPh)$,

Z-Leu-Phe-$CH_2CH(OH)C_6H_4(4\text{-}N(CH_3)_2)$,

Z-Leu-Abu-CH_2-2-pyridyl,

Z-Leu-Abu-$(CH_2)_2O(CH_2)_2OH$,

Z-Leu-Phe-CH_2-2-pyridyl,

Z-Leu-Abu-$(CH_2)_2$NH-biotinyl,

Z-Leu-Abu-$CH_2\text{-}C_6H_{11}$,

Z-Leu-Phe-$CH_2CH(OH)C_6F_5$,

Z-Leu-Abu-CH_2-2-furyl,

Z-Leu-Abu-$(CH_2)_3C_6H_5$,

Z-Leu-Abu-$(CH_2)_2OH$,

Z-Leu-Abu-$CH_2CH(OH)C_6H_4(3\text{-}OPh)$,

Z-Leu-Abu-$(CH_2)_2$-4-morpholinyl,

Z-Leu-Abu-$CH_2CH(OH)Ph$,

Z-Leu-Abu-CH_2-4-pyridyl,

Z-Leu-Abu-$(CH_2)_3$-1-pyrrolidine-2-one,

Z-Leu-Phe-$CH_2CH(OH)Ph$,

Z-Leu-Abu-$CH_2C_6H_3(3,5\text{-}(OCH_3)_2)$,

Z-Leu-Nva-$CH_2CH(OH)Ph$,

Z-Leu-Abu-CH_2-8-caffeinyl,

Z-Leu-Abu-*n*-Pr,

Z-Leu-Abu-CH_2-3-pyridyl, and

Z-Leu-Phe-CH_2Ph.

5. A method for treating neuropathy comprising administering to a patient an amount of Z-Leu-Abu-$(CH_2)_3$-4-morpholinyl effective to inhibit axonal degeneration.

6. The method of claim 5, wherein the neuropathy is selected from the group consisting of chronic degeneration of motor and or sensory neurons, idiopathic peripheral neuropathies, peripheral neuropathies due to genetic mutations, peripheral neuropathies, uremia, rheumatologic diseases, liver diseases, infections, axonal degeneration secondary to primary demyelinating disorders, inflammatory demyelinating neuropathies, multiple sclerosis, and chronic spinal cord degenerations.

7. A method for treating a hyperproliferative disorder comprising administering to a host an anti-hyperproliferative agent in combination with a calpain inhibitor.

8. The method of claim 7, wherein the hyperproliferative disorder is cancer.

9. The method of claim 7, wherein the calpain inhibitor is a peptide α-ketoamide.

10. The method of claim 7, wherein the anti-hyperproliferative agent is paclitaxel.

11. A pharmaceutical composition comprising an anti-hyperproliferative agent in combination with a calpain inhibitor.

12. The composition of claim 11, wherein the calpain inhibitor is a peptide α-ketoamide.

13. The composition of claim 12, wherein the peptide α-ketoamide comprises the compound of claim 1.

14. The method of claim 11, wherein the anti-hyperproliferative agent is paclitaxel.

15. Method of treating chemically-induced neuropathy, comprising

administering an amount of a calpain inhibitor to a host effective to inhibit chemically-induced axonal degeneration.

16. The method of claim 15, wherein the neuropathy is induced by an anti-hyperproliferative agent.

17. The method of claim 16, wherein said neurotoxin comprises a microtubule stabilizing agent.

18. The method of claim 17, wherein said microtubule stabilizing agent comprises paclitaxel.

19. A method for treating calcium-induced cell injury comprising:

contacting a nerve cell with an amount of a calpain inhibitor effective to modulate chemically-induced axonal degeneration.

20. The method of claim 19, wherein the calpain inhibitor comprises a peptide α-ketoamide.

21. The method of claim 20, wherein the peptide α-ketoamide comprises the compound of claim 1.

22. The method of claim 19, wherein the calpain inhibitor comprises Z-Leu-Abu-CONH-$(CH_2)_3$-4-morpholinyl.